

Amendments to the Specification

Please insert the Substitute Sequence Listing provided herewith on pages 1-5 after the claims of the application.

At page 6, lines 7-24, please replace the first paragraph under the heading, "Example 1: Cloning of the GORI-28/ChemR23 receptor," with the following paragraph:

GORI-28 was described by Samson et al. (1998) as ChemR23 and by Methner et al. (1997) as DEZ, and several data base entries exist. The analysis of a genomic clone (Genbank Accession No. NT_009660.4) showed that the described variants of DEZ isoform A (Genbank Accession No. U79526) and isoform B (Genbank Accession No. U79527) are the products of alternative splicings. DEZ isoform A is identical in amino acid sequence with ChemR23 and DEZ isoform B, the N terminus of isoform A being extended by two amino acids, methionine and arginine. To enable simplified cloning from genomic DNA, a genomic clone for ChemR23/DEZ isoform B, which obtained the designation GORI-28, was produced *in silico*. As compared to the sequence of ChemR23 (Genbank Accession No. Y14838), GORI-28 contains a guanine in position 900, which represents a silent mutation, and from position 1294, it has a sequence which completely differs from the published sequence. The cDNA for GORI-28 was amplified from genomic DNA by PCR using the primers 5' TGG TCC CTG TCT TCT CTT GC 3' (GORI28oli1) [SEQ ID NO: 15] and 5' TGT CCC TGG GTT GAG AGA GT 3' (GORI28oli2) [SEQ ID NO:16] to obtain a 1186 bp fragment which was subsequently subcloned into the expression vector pCI or other usual expression vectors. The sequence was checked by DNA sequence analysis and confirmed.

At page 9, line 22, through page 10, line 2, please replace the paragraph with the following paragraph:

The purity of COM was checked by capillary zone electrophoresis (P/ACE 2000, Beckman) (not shown). The determination of the molecular mass was effected by a Voyager DE PRO mass spectrometer (PerSpective), and a mass of 15,562 Da was established. The N terminus and the first 33 amino acids were determined by Edman degradation (Applied Biosystems Gas Phase Sequencer 473 A). From these data, the amino acid sequence of COM with 134 amino acids and a theoretical molecular weight of 15,566 Da can be derived, taking into account that the six cysteine residues form three disulfide bridges. The amino acid sequence [SEQ ID NO:1] determined of COM reads:

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1  ELTEAQRRLGL QVALEEFHKKH PPVQWAFQET SVESAVDTPF PAGIFVRLEF
51  KLQQTSCRKR DWKKPECKVR PNGRKRKCLA CIKLGSEDKV LGRLVHCPIE
101 TQVLREAEEH QETQCLRVQR AGEDPHSFYF PGQF

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At page 10, lines 7-17, please replace the paragraph under the heading, "Example 6: Cloning and recombinant expression of TIG2 in CHO cells," with the following paragraph:

The cDNA for human TIG2 (Genbank Accession No. U77594) was amplified from liver cDNA by PCR with the primers 5' GCCAGGGTGACACGGAAG 3' (TIG2oli1) [SEQ ID NO:3] and 5' GAGGCACCACGCAGCTC 3' (TIG2oli2) [SEQ ID NO:4] to obtain a fragment of 537 bp, which was subcloned into the vector pGEM5Zf-T or other usual vectors. The sequence was checked by DNA sequence analysis and confirmed. From this recombinant vector, a fragment which contains the cDNA of TIG2 was excised with suitable restriction enzymes and subcloned into the expression vector pCI or other usual expression vectors. CHO cells were transfected with the recombinant expression vector as

in Example 2, and stable cell clones were selected as in Example 2. The cell clones obtained were examined for the expression of TIG2 by RT-PCR.

At page 11, lines 2-21, please replace the paragraph under the heading,
"Example 8: Cloning and recombinant expression of COM in yeast," with the following paragraph:

By PCR with the primers 5' CTCTCGAGAAAAGAGAGCTCACGGAAGCCCAGC 3' (COMoli1) [SEQ ID NO:5] and 5' TTGTCGACTTAGAACTGTCCAGGGAAGTAGAAGC 3' (COMoli2) [SEQ ID NO:6] and using the TIG2 cDNA cloned in Example 6, a 427 bp fragment which represents the cDNA for COM was amplified and subsequently subcloned into the vector pGEM5Zf-T or other usual vectors. After confirming the sequence by DNA sequence analysis, a fragment was excised from the recombinant vector by means of suitable restriction enzymes and subcloned into the modified yeast expression vector YEpFLAG-1 or other usual expression vectors. The yeast strain BJ3505 or other usual yeast strains were transformed with the expression construct by electroporation. The thus formed ADH2+ clones were checked by PCR analysis for insertion of the COM DNA into the yeast genome. For the preparation of recombinant COM, 10 ml cultures were inoculated with COM-positive clones, and expression was induced. After 96 h, the cell supernatants were harvested and tested for expression of the recombinant COM after separation through a gel (SDS PAGE) and staining with Coomassie blue. In the yeast expression system described, the cDNA of COM is fused to the N-terminal signal of the yeast alpha factor. The alpha factor signal sequence causes the fusion product to be secreted into the cell medium. The alpha factor signal sequence is cleaved off by the endogenous protease Kex 2 to form mature COM.

At page 13, lines 2-16, please replace the first paragraph under the heading, "Example 12: Expression of TIG2 and GORI-28 in selected cell lines," with the following paragraph;

The native expression of TIG2 and GORI-28 in various cell lines was examined by RT-PCR with gene-specific primers. COM was amplified with the TIG2oli1 and TIG2oli2 pair of primers (see Example 6) as a 537 bp cDNA fragment and isolated by gel electrophoresis. By analogy, GORI-28 was amplified and detected by means of the primer pair 5' GGC CAT GTG CAA GAT CAG CAA CT 3' (mDEZoli1) [SEQ ID NO:7] and 5' AGA ATG GGG TTC ATG CAG CTG TT 3' (mDEZoli2) [SEQ ID NO:8] as a 618 bp fragment; for the PCR amplification from murine adipocytes, the primer pair 5' TCT ACA ACG GTG GAA CAG TGA 3' (mDEZoli3) [SEQ ID NO:9] and 5' AAG AAA GCC AGG ACC CAG A 3' (mDEZoli4) [SEQ ID NO:10] was employed to form a 536 bp fragment; for the amplification from human dendritic cells, the primer pair 5' CAG ACA ACA TAA CGG TGA ATG A 3' (hDEZ_a_Oli5) [SEQ ID NO:11] and 5' AAG AAA GCC AGG ACC CAG A 3' (hDEZ_a_Oli4) [SEQ ID NO:12] was employed to form a 524 bp fragment. From cell samples of the cells to be examined, RNA was isolated by the usual methods, then transcribed into a first strand cDNA which was employed for PCR amplification.

At page 14, lines 10-25, please replace the first paragraph under the heading, "Example 13: Expression of COM and GORI-28 in skin cells from patients with sin diseases," with the following paragraph:

As described in Example 12, the expression of COM and its receptor GORI-28 was established by RT-PCR. For the amplification of GORI-28, in this case, the primer pair

5' GCA CAG CAT CAC TTC TAC CAC TT 3' (hDEZoli3) [SEQ ID NO:13] and 5' CTG TAG ACC ACC ACC AGG AAG A 3' (hDEZoli2) [SEQ ID NO:14] was used to form a 324 bp fragment. Skin punches from patients with no skin disease (control, C) and from patients suffering from psoriasis (Pso) or atopic dermatitis (AD) were obtained from a skin hospital. The material was prepared by the usual methods to isolate RNA, from which a first strand cDNA was in turn synthesized as described in Example 12 and employed for PCR amplification. The receptor GORI-28 is expressed both in the skin tissue of healthy subjects and in the skin tissue of patients with psoriasis or atopic dermatitis (see Figure 10 A). In contrast, COM expression could be detected only in the tissue of healthy subjects, but not in the skin tissue of patients who suffer from psoriasis or atopic dermatitis (see Figure 10 B). Thus, the lack of COM expression is in a causal relationship with skin diseases and indicates a therapeutic effectiveness of COM for this field of indications.